

INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY
IN THE EUROPEAN PATENT OFFICE
UNDER THE PATENT COOPERATION TREATY

In re International application of)
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 EXPONENTIAL BIOTHERAPIES, INC. et al.)
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 Int'l. Application No.:PCT/US03/21061) BOX: PCT
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 Int'l. Filing Date: July 7, 2003)
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 For: VIRULANT PHAGES TO CONTROL)
 LISTERIA MONOCYTOGENES IN FOOD)
 STUFFS AND IN FOOD PROCESSING)
 PLANTS)

CONFIRMATION

International Preliminary Examining Authority
European Patent Office
Erhardstrasse 27
D-80331 Munich
Germany

June 7, 2004

**AMENDMENT OF INTERNATIONAL
APPLICATION UNDER PCT ARTICLE 34, RULE 66.3**

The attached replacement pages including amendments to this International Application and the following comments are submitted in response to the Written Opinion of March 8, 2004.

Applicants respectfully request consideration of these amendments and the following comments in the establishment of a favorable International Preliminary Examination Report.

EXPLANATION OF AMENDMENTS TO THE APPLICATION

Claim 1 has been amended to indicate that the lytic phage is P100.

Original Claim 2 has been deleted.

Claims 3-48 have been renumbered as claims 2-47 and the dependencies of the claims have been changed accordingly.

Claim 35 (renumbered as claim 34) has been amended to indicate that the endolysin protein is "derived" from phage P100 instead of "obtainable" from P100.

Claim 39 (renumbered as claim 38) has been amended to delete the language "by another bacterial species".

Claim 43 (renumbered as claim 42) has been amended to indicate that the endolysin protein is "derived" from phage P100 instead of "obtainable" from P100.

Page 2 of the specification has been amended to recite references D2-D5.

COMMENTS ON NOVELTY AND INVENTIVE STEP

In the Written Opinion mailed March 8, 2004, the Examiner indicated that claim 1 lacked novelty under PCT Article 33(1) in view of reference D1. Claim 1 has been amended to indicate that the lytic phage is phage P100. Since the Written Opinion indicates that the feature "phage P100" is novel in view of the documents of the search report, the presently amended claims are novel over reference D1.

In the Written Opinion, the Examiner further indicated that claims 35 and 43 (renumbered as claims 34 and 42) should be amended to indicate that the endolysin is derived from phage P100. The claims have been amended as suggested, however, applicants respectfully point out that the endolysin is derived from phage P100 but could be recombinantly produced.

The Written Opinion states that claim 39 is vague and unclear. Claim 39 has been renumbered as claim 38 and amended to delete the language "by another bacterial species". Applicants believe that claim 38 now clearly defines the claimed subject matter.

The Written Opinion requests that the background art disclosed in references D2-D5 be identified in the description. Page 2 of the description has been amended to recite these references.

The Written Opinion requests that the number of independent claims be reduced. Claims 23 and 43 (renumbered as claims 22 and 42) have been changed to dependent claims.

For all of the above reasons, Applicant respectfully contends that the subject matter of each of the claims is both novel and inventive and the establishment of an International Preliminary Examination Report indicating such is requested.

Respectfully submitted,

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Attachments (Replacement Pages 2, 2A, 19-23)

The present invention concerns the use of a recently discovered Listeria phage with specific, essential and relevant properties, which makes it particularly suitable for identifying and controlling Listeria contamination of dairy products, facilities and equipment.

In addition to the general scientific literature on the subject, there is also patent literature that teaches the utility of phages in general to control bacterial contaminations in food processing plants and in foodstuffs. See for example U.S. Patent No. 5,006,347 issued on April 9, 1991, U.S. Patent No. 4,851,240 issued on July 25, 1989, GB 2 253 859 A published on September 23, 1992 and EP 0414304A2 published on February 27, 1991. However, none of the above discussed patents disclose a Listeria phage which was actually tested and shown to successfully control bacterial contamination in food processing plants and in food products. The reason for this is that all of the Listeria phages known in the art at the time of the disclosure in the previous patents were temperate phages, and were therefore not efficient at nor suitable for industrial bacterial eradication purposes. The term "temperate" refers to the fact when a strain of phage injects its DNA into a bacterial target, the phage DNA integrates into the DNA of the host cell, as a "prophage", and can remain integrated therein for considerable periods of time. Since the prophage excises (and initiates replication and lysis) only when the host cell becomes stressed, the ensuing bacterial lysis is unpredictable and not easily controlled, which is why temperate phages do not lend themselves well to industrial applications. Temperate phages are unsuitable for industrial decontamination purposes for other reasons as well, including the fact that they can deliver unwanted and dangerous genes to the bacteria target into which their DNA integrates. In contrast, there is a class of phages that lyse bacterial targets directly, given that they do not have the molecular machinery required to integrate into the bacterial targets. Such phages are referred to as being "virulent" or "lytic" for the bacterial targets. Virulent phages against Listeria monocytogenes were discovered recently, by one of the present inventors.

The first of these virulent Listeria phages, designated A511, was described in the literature in 1990 (see Loessner et. al., Applied and Environmental Microbiology, June 1990, p.1912-1918, 1990). See also DE 43 26617 C; Loessner et. al., Applied and Environmental Microbiology, April 1996, vol. 62, No. 4, p.1133-1140; and Gaeng et al., Applied and Environmental Microbiology, July 2000, vol. 66, No. 7,

p.2951-2958. The virulent phage according to the present invention belong to the Myoviridae family and have tails which contract towards the virus head. One particularly preferred phage is designated P100 and was deposited at the

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